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EXAMINER	
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ART UNIT	PAPER NUMBER
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/28/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/721,144	HARIRI, ROBERT J.	
	Examiner	Art Unit	
	Laura McGillem .	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6,8,12-13,15-18,20-23,31,32,34-37 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,6,8,12-13, 15-18,20-23,31-32,34-37 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

It is noted that claims 1, 3, 18, 31, 34 and 50 have been amended and claims 2, 4 and 9 have been cancelled in the response filed 10/5/2006. Claims 1, 3, 5-6, 8, 12-13, 15-18, 20-23, 31-32, 34-37 and 50 are under examination.

Claim Rejections - 35 USC § 112

Claims 1 and 50 have been amended to remove an indefinite phrase, therefore rejection of claims 1, 3, 5-6, 8, 12-13, 15-17 and 50 under 35 U.S.C. 112 second paragraph has been withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 5-6 and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 10 and 13-14 of copending Application No. 10/366,671 in view of Erices et al (Br. J. Haematol., 2000 Vol. 109, No.1, abstract). The claims are not patentably distinct from one another because the product of the instant claims is an obvious variation of the composition of copending Application No. 10/366,671.

This is a provisional obviousness-type double patenting rejection.

Instant claim 1 is drawn to cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells comprising at least about one hundred $CD34^+$ cells or at least about one hundred $CD8^+$ cells within a plurality of potent cells, and the unit comprising cells from a plurality of sources, wherein one source of said plurality of sources is postpartum placenta perfusate. Instant claim 3 is drawn to the unit wherein the unit comprises pluripotent cells from fetal cord blood. Claim 18 is drawn to a cytotherapeutic unit comprising at least two types of potent cells. The instant claims do not specifically recite a unit comprising placental stem cells that are $SH2^+$, $SH3^+$ and $SH4^+$.

Conflicting claim 1 is drawn to a composition comprising human stem or progenitor cells and isolated placental stem cells that are $SH2^+$, $SH3^+$ and $SH4^+$, wherein said placental stem cells are obtained from a placenta that has been drained of cord blood and flushed to remove residual blood. Conflicting claim 2 is drawn to a composition comprising human umbilical cord blood stem cells and placental stem cells that are $SH2^+$, $SH3^+$ and $SH4^+$, wherein said placental stem cells are obtained from a

placenta that has been drained of cord blood and flushed to remove residual blood. Conflicting claims 10, 13 and 15 are drawn to a composition wherein the stem or progenitor cells are from fetal or neonatal hematopoietic stem or progenitor cells, adult cells or bone marrow stem or progenitor cells, or umbilical cord blood or placental blood, including umbilical cord blood stem cells wherein a plurality of cell are CD34+ and CD38+. The conflicting claims do not recite a limitation of the composition of at least about one hundred CD34+ cells or at least about one hundred CD8+ cells.

Erices et al teach that mesenchymal progenitor cells from cord blood comprise an antigenic profile of $SH2^+$, $SH3^+$ and $SH4^+$ and give rise to marrow stroma (see abstract). Therefore, the claimed cytotherapeutic unit comprising cells from a placenta perfusate and fetal cord blood would inherently have stem cells that are $SH2^+$, $SH3^+$ and $SH4^+$.

It would have been obvious to one of skill in the art at the time the invention was made to make a cytotherapeutic unit for treatment of a patient in need of hematopoietic cells comprising at least about one hundred CD34+ cells or at least about one hundred CD8+ cells in order to have a sufficient hematopoietic cell population for therapeutic purposes. The motivation to do so would be the expected benefit of being able to administer a sufficient amount of hematopoietic cells for patient treatment since umbilical cord blood samples are known in the art to contain a relatively low number of cells in a small volume. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that

said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

It is noted that the limitation of "plurality of sources" in claims 1, 18, 31 and 34 have been amended to postpartum placenta perfusate.

The rejection of claims 1, 3, 5-6, 8, 12, 15-18, 20-23, 31-32, 34-35 and 37 under 35 U.S.C. 102(e) as being anticipated by Pykett et al (U.S Patent No. 6,548,299) has been withdrawn.

The rejection of claims 1, 3, 5-6, 8, 15-18, 20-23, 31-32, 34-35 and 37 under 35 U.S.C. 102(b) as being anticipated by Johnson et al (U.S Patent No. 5,677,139) has been withdrawn.

Claims 1, 3, 5-6, 8, 15-18, 20-23, 31-32, 34, 36-37 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Fasouliotis et al (Eur. J. Obstet. Gynecol. Reprod. Biol. 2000, Vol. 90, pages 13-25).

Fasouliotis et al teach methods of collection and storage of hematopoietic cells for patients with major hematological disorders (i.e. a patient in need of hematopoietic

cells). Fasouliotis et al teach methods of collecting cells including collecting umbilical cord blood using a syringe before placental delivery. Fasouliotis et al also teach that cells can be collected by flushing the delivered placenta with saline and retrieving blood by syringe (see pages 15, right column and Table 2 for example), which reads on a cytotherapeutic unit comprising cells from a plurality of sources wherein one source is cells from the postpartum placenta, and postpartum placenta perfusate (e.g. blood and saline) and another source is fetal cord blood as claimed in claims 5-6 and 8. As written, claim 1 does not place any limitation on the kind of cell that would come from a postpartum placenta perfusate.

Fasouliotis et al teach that umbilical cord blood contains about 8,000 erythroid progenitor cells/ml, 13,000-24,000 myeloid progenitor cells/ml and 1000-10,000 multipotent progenitor cells/ml (see page 17, right column, 3rd paragraph, for example). Fasouliotis et al teach that the CD34 antigen is a defining hallmark of hematopoietic stem/progenitor cells and that it is possible to achieve separation of a highly enriched population of CD34+ cells from cord blood using immunoselection (see page 18, left column, 2nd paragraph, for example). Absent evidence to the contrary, the samples taught by Fasouliotis et al would comprise at least about one hundred CD34+ cells. Therefore, the blood samples taught by Fasouliotis et al anticipate a cytotherapeutic unit suitable for patient treatment in need of hematopoietic cells comprising cells from a plurality of sources wherein one source is postpartum placenta perfusate and the unit comprises at least about one hundred CD34+ cells.

Absent evidence to the contrary, erythroid progenitor cells, myeloid progenitor cells and multipotent progenitor cells (see page 17, right column, 3rd paragraph, for example) are pluripotent cells and meet the limitation of claim 3. Fasouliotis et al teach that immunoselection can be used to separate a highly enriched population of CD34+ cells from the cord blood (see page 18, left column, 2nd paragraph, for example) which reads on selection of a potent cells to render the unit suitable for therapy for an indicated disease as in claim 16 and also meets the limitations of claims 15, 17 and 31 wherein at least one type of cell is excluded or removed from the unit (on the basis of not expressing CD34). Fasouliotis et al further teach that the hematopoietic cells can be separated based on expression of both CD45RA and CD71 antigens (see page 18, left column, 2nd paragraph, for example), which reads on the claimed cytotherapeutic unit comprising at least two preselected types of potent cells (claim 18). Fasouliotis et al teach that separation of mononuclear cells from red blood cells and polymorphonuclear leukocytes reduces the volume of stored cells and allows the storage of large numbers of cord blood samples in minimal space without the need for freezing un-separated blood bags (see page 16, left column, 3rd-5th paragraphs, for example). The blood sample taught by Fasouliotis et al that has been depleted of RBC followed by CD34, CD45RA and CD71 selection meets the limitation of a cytotherapeutic unit wherein at least one type of cell and a plurality of cell types (i.e. RBC and any cell not expressing the selected antigenic determinants) have been removed from the unit and anticipates claims 31-32.

Fasouliotis et al discloses that hematopoietic cell can be obtained from umbilical cord and from a saline perfusion of post partum placenta. Absent evidence to the contrary, at least one of the cell types (CD34+, CD45RA and CD71) would be obtained from the placenta perfusion while at least one of the other cell types would be obtained from the blood from the umbilical cord (i.e. a source of another type) and would meet the limitation of claim 34. The CD34+ cells or CD45RA+ /CD71+ cells meet the limitation of claim 37, of cells in a cytotherapeutic unit wherein at least one of the cells has been characterized.

Fasouliotis et al teach that the blood samples can be cryopreserved with a cryoprotectant before use (see page 16, right column, 4th paragraph, for example), which meets the limitation of a cytotherapeutic unit in a frozen state and anticipates claim 36. Fasouliotis et al teach that large-scale collection and storage of umbilical cord has been established in worldwide umbilical cord blood banks (i.e. libraries). Fasouliotis et al teach that such banks reduce the time from donor search initiation to stem cell acquisition, reduces risks associated with unrelated donor bone marrow transplantation, and could help alleviate under-represented minority donor cell supply (see page 22, right column, 3rd paragraph, in particular). Therefore, the cord blood banks taught by Fasouliotis et al meet the limitation of claim 50 of a library of cytotherapeutic units.

Claims 20-22 are drawn to the cytotherapeutic unit distributed with a certification of the contents of the unit, such as indication of cells excluded or absent from the unit. Claim 23 is drawn to the unit with certification that indicates how the contents of the unit render it suitable for therapy for an indicated disease or condition. Claim 50 is drawn to

a unit that has been assayed to ensure the accuracy of the identities and numbers of at least some of the plurality of cells. These limitations appear to be drawn to knowledge concerning the cytotherapeutic unit, wherein the knowledge is certification (e.g. assurance) of the contents of the unit. The identities and numbers of at least some of the cells in the cytotherapeutic unit is an inherent property of the unit. Whether the assay to determine the identities and numbers of the cells is accurate or not is an inherent property of the assay. Absence of particular cell types from a cytotherapeutic unit, whether deliberately excluded or not present to begin with, is an inherent property of the cytotherapeutic unit. In other words, certain cell types are present in the unit or they are not. Either the particular cytotherapeutic unit for an indicated disease state or condition is suitable based on the cell content or it is not suitable. Knowledge or certification of the excluded or absent cells does not alter the properties of the claimed cytotherapeutic unit. Likewise, certification of the suitability of the cytotherapeutic unit does not change the properties of the unit.

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.") See MPEP 2112.

Therefore, the hematopoietic cell in the preparations taught by Fasouliotis et al would have numbers and identities, and the assays performed by Fasouliotis et al to

determine numbers and viability would or would not be accurate. In order for the hematopoietic cell preparations taught by Fasouliotis et al to anticipate the claimed cytotherapeutic unit, it is not necessary for the Fasouliotis et al to have known the identities and numbers of at least some of the plurality of cells or to know or certify the accuracy of the assay. It is not necessary for the Fasouliotis et al to specifically certify which cells are absent or have been excluded or whether the preparation of cells or matrix with cells is suitable for treating a subject for the preparation to anticipate the claimed unit.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1, 3, 5-6, 8, 12, 15-18, 20-23, 31-32, 34- 37 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pykett et al (U.S. Patent No. 6,548,299, of record) in view of Fasouliotis et al (Eur. J. Obstet. Gynecol. Reprod Biol., 2000, Vol. 90, pages 13-25).

Pykett et al teach a population of cells obtained from blood products comprising hematopoietic cells, including $CD34^+$ cells. Pykett et al teach that the cells can be used to supplement or replenish a patient's hematopoietic progenitor cell population (see column 19, lines 12-25, for example), which reads on a cytotherapeutic unit suitable for

treatment of a patient in need of hematopoietic cells. Pykett et al teach embodiments wherein the hematopoietic cells are pluripotent or multipotent cells and may obtained from bone marrow, peripheral blood, umbilical cord blood, placental blood, fetal liver and lymphoid soft tissue (see column 3, lines 37-50). Pykett et al teach that five to ten milliliters of blood were extracted from an umbilical cord prior to infant delivery. After delivery, the placenta was removed and blood contained in the placenta was collected. Pykett et al teach that the cord blood and placenta blood were mixed together before processing (see column 31, lines 10-25, in particular), which reads on cells from a plurality of sources wherein one source is fetal cord blood or post-partum placenta. Pykett et al teach an embodiment in which five thousand CD34+ cells are co-cultured with thymic stromal cells and after 7 days, the CD34+ were harvested. Since the culture taught by Pykett et al started with five thousand CD34+ before expansion, absent evidence to the contrary, after harvest there would be at least about one hundred CD34+ cells.

Pykett et al teach that the blood products can be fractionated or enriched. Pykett et al teach that the blood was centrifuged to separate mononuclear cells and then remaining erythrocytes were lysed, which reads on exclusion of at least one type of cell from the unit and meets the limitation of claim 15. The cell preparation taught by Pykett et al is obtained by separating CD34+ cells from the blood products. Pykett et al teach that CD34+ cells were isolated using a CD34 progenitor cell selection system comprising mixing the cell sample with anti-human CD34 beads (see column 31, lines 10-40, for example). For example, mature differentiated cells can be selected against or

CD34+ cells can be selected from the population of cells in the blood product by using paramagnetic anti-CD34 beads (see column 12, lines 31-50, for example). Subsequently, the harvested cells were counted, assessed for viability and the presence of CD34 was checked using anti-CD34 antibodies in flow cytometry analysis (see column 33, lines 10-60, in particular) which reads on cell identities reflecting the presence or absence of at least one antigenic determinant (e.g. CD34+), and also selection of the plurality of potent cells to render the unit suitable for therapy for an indicated disease or condition such as a patient with an immunodeficiency (see column 9, lines 20-30 and column 19, lines 12-20, for example) and meet the limitation of claims 16-17.

Pykett et al teach that further immunomagnetic methods, using an antibody to the stem cell antigen AC133, were used to select for an immature phenotype of progenitor cells (see column 32, lines 37-59, in particular), which reads on a AC133 as a second preselected type of cell for the hematopoietic population and meets the limitation of claim 18.

Pykett et al teach that the cells can be co-cultured with lymphoreticular stromal cells on a biocompatible matrix obtained from lymphoid tissue in order to expand and direct differentiation of the hematopoietic cells (see column 12, 53-67 lines and column 13, lines 1-11). Pykett et al teach that the lymphoreticular stromal cells can be non-autologous, or from a subject (source) different from the subject (source) of the hematopoietic cells (see column 27, lines 21-43, for example) and meets the limitation of claim 34. Pykett et al disclose that lymphoreticular stromal cells can be obtained from

lymphoid tissue and cryopreserved for later use (see column 14, lines 14-30, for example), which reads on the claimed cytotherapeutic unit wherein at least one type of cell is frozen separately from another type of cells (e.g. CD34+ cells) and wherein at least one of said cells has been characterized (i.e. is of lymphoid origin) as in claims 35-36. In addition, Pykett discloses that unfractionated blood products can be retrieved from cryopreservative storage (see column 12, lines 50-53, for example). Pykett et al further teach that the entire matrix, lymphoreticular stromal cells and hematopoietic cells can be implanted into subjects (see column 2, lines 50-67, for example).

Claims 20-22 are drawn to the cytotherapeutic unit distributed with a certification of the contents of the unit, such as indication of cells excluded or absent from the unit. Claim 23 is drawn to the unit with certification that indicates how the contents of the unit render it suitable for therapy for an indicated disease or condition. Claim 50 recites the limitation that "each of said units being assayed to ensure the accuracy of said identities and numbers of at least some of the plurality of potent cells comprising said unit". These limitations appear to be drawn to knowledge concerning the cytotherapeutic unit, wherein the knowledge is certification (e.g. assurance) that the assay is accurate. The identities and numbers of at least some of the cells in the cytotherapeutic unit is an inherent property of the unit. As discussed above, whether the assay to determine the identities and numbers of the cells is accurate or not is an inherent property of the assay. Absence of particular cell types from a cytotherapeutic unit, whether deliberately excluded or not present to begin with, is an inherent property of the cytotherapeutic unit. In other words, certain cell types are present in the unit or they are not. Either the

particular cytotherapeutic unit for an indicated disease state or condition is suitable based on the cell content or it is not suitable. Knowledge or certification of the excluded or absent cells does not alter the properties of the claimed cytotherapeutic unit. Likewise, certification of the suitability of the cytotherapeutic unit does not change the properties of the unit. See MPEP 2112. Therefore, the hematopoietic cell in the preparations taught by Pykett et al would have numbers and identities, and the assays performed by Pykett et al to determine numbers and viability would or would not be accurate. It is not necessary for the Pykett et al to have known the identities and numbers of at least some of the plurality of cells or to know the accuracy of the assay.

Pykett et al does not teach a library of cytotherapeutic units. Pykett et al does not teach that a source of hematopoietic cells is a postpartum placenta perfusate.

The teaching of Fasouliotis et al has been discussed in the above rejection. Specifically, Fasouliotis et al teach that large scale collection and storage of umbilical cord has been established in worldwide umbilical cord blood banks (i.e. libraries). Fasouliotis et al teach that such banks reduce the time from donor search initiation to stem cell acquisition, reduces risks associated with unrelated donor bone marrow transplantation, and could help alleviate under-represented minority donor cell supply (see page 22, right column, 3rd paragraph, in particular). Fasouliotis et al teach methods of collecting umbilical cord blood for storage including collection of the blood using syringes before placental delivery, and optionally flushing the delivered placenta with saline in order to retrieval additional blood (see pages 15, right column and Table 2 for example). Fasouliotis et al teach that a disadvantage of using umbilical cord blood is the

relatively low number of nucleated cells in the average donation, and the scarcity of cells potentially limit wide spread therapeutic use of cord blood (see page 18, left column, 3rd paragraph for example).

It would have been obvious to the skilled artisan at the time the invention was made to produce a library or bank of the donor samples such as taught by Pykett et al because Fasouliotis et al teach that many blood samples can be collected from cord blood and a saline flush of postpartum placenta, enriched for CD34+ cells and stored in a bank so that they will be available for a patient in need of hematopoietic cells. The motivation to make a library or bank of the donor samples as taught by Fasouliotis et al are the expected benefits of having easy access to blood samples, increased speed of donor search, viral safety and having a source of stem cells for expansion and gene therapy. A further benefit would be the ability to expand available donor pools in currently under-represented ethnic and racial minorities (see page 14, left column, 3rd paragraph, for example). There is a reasonable expectation of success in making a library or bank of the cytotherapeutic units taught by Pykett et al since it has worked previously as described by Fasouliotis et al.

It would also have been obvious to the skilled artisan at the time the invention was made to perfuse the postpartum placenta as taught by Fasouliotis et al to collect cells for a therapeutic cell composition such as produced by Pykett et al because Fasouliotis et al teach that there is a relatively small number of cells in a sample of umbilical cord blood. The motivation to use postpartum placenta perfusate is the expected benefit of being able to collect additional blood as disclosed by Fasouliotis et

al (see Table 2, page 15, in particular). There is a reasonable expectation of success in using postpartum placenta perfusate to increase cell number in cytotherapeutic units since it has worked previously as described by Fasouliotis et al. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 1, 3, 5-6, 8, 12, 15-18, 20-23, 31-32, 34- 37 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pykett et al (U.S. Patent No. 6,548,299, of record) in view of Wang et al (Blood, 2001 Vol. 98 (No. 11 Part 1) page 193 (abstract only)).

The teachings of Pykett et al are described in the above rejection. Pykett et al do not teach a cytotherapeutic unit comprising cell from postpartum perfusate.

Wang et al teach a method to recover mononucleated cells and hematopoietic progenitor and stem cells (HPSC) from postpartum human placenta by perfusing the placenta to remove residual blood, and then continuously perfusing at a controlled rate until 200 to 250 ml of postpartum placenta perfusate was collected. Wang et al teach that populations of HPSC that were characterized as $CD34^+$ $CD38^+$ cells were recovered in numbers comparable to the number of cells recovered from a typical unit of umbilical cord blood, but with a significantly higher proportion of $CD34^+CD38^-$ cells. Wang et al conclude that HPSC from postpartum placenta may be used to supplement

umbilical cord blood to yield sufficient graft material for transplantation into adults (see full abstract, in particular).

It would have been obvious to the skilled artisan at the time the invention was made to collect hematopoietic cells from a postpartum placenta perfusate as taught by Wang et al to add to a cell sample for therapeutic use as taught by Pykett et al because Wang et al teaches that postpartum placenta perfusate yields a useful quantity of $CD34^+CD38^-$ cells, which is a cell subpopulation believed to contain long term repopulating activity. The motivation to use postpartum placenta perfusate as an additional source of $CD34^+$ hematopoietic cells for a therapeutic transplant sample is the expected benefit of being able to have a sufficient volume of therapeutic cells to meet the cell dose requirements of adult hematopoietic cell transplant recipients as suggest by Wang et al. There is a reasonable expectation of success to collect and use cells from a postpartum placenta perfusate for a cytotherapeutic unit since it has worked previously in the cited reference. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1-6, 8, 15-18, 20-23, 31-32, 34-35, 37 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (U.S Patent No. 5,677,139), of record) in view of Fasouliotis et al (Eur. J. Obstet. Gynecol. Reprod Biol., 2000, Vol. 90, pages 13-25).

Johnson et al teach a population of cells comprising hematopoietic cells, including CD34+ cells, obtained from blood products. Johnson et al teach that the cells can be used for immune supplementation for a patient undergoing chemotherapy or radiation therapy (see column 9, lines 24-34, for example), which reads on a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells. Johnson et al teach embodiments wherein the hematopoietic cells are human pluripotent cells and may obtained from bone marrow, peripheral blood, umbilical cord blood, or peripheral blood mobilized stem cells (see column 5, lines 4-17). Johnson et al teach that five milliliters of venous blood were extracted from an umbilical cord prior to infant delivery. After delivery, the blood contained in the placenta was collected. Johnson et al teach that the cord blood and placenta blood were mixed together before processing (see column 10, lines 24-34, in particular), which reads on cells from a plurality of sources and wherein one source is fetal cord blood or post-partum placenta. Johnson et al teach that CD34+ cells were isolated using a CD34 progenitor cell selection system comprising mixing the cell sample with anti-human CD34 beads so that cells not bound to the paramagnetic beads could be removed (see column 10, lines 53-67 and column 11, lines 1-32, for example). Since the culture taught by Johnson et al started with 10^3 to 10^5 $CD34^+$ cells per well before expansion, absent evidence to the contrary, after harvest there would be at least about one hundred $CD34^+$ cells.

Johnson et al teach that the blood was centrifuged to separate mononuclear cells and then remaining erythrocytes were lysed, which reads on exclusion of at least one type of cell from the unit and meets the limitation of claim 15. Johnson et al teach an

embodiment in which $CD34^+$ cells are co-cultured with thymic stromal cells at a concentration of 10^3 to 10^5 $CD34^+$ cells/well for expansion and differentiation (see column 12, lines 19-32, for example). Subsequently, the identity of the cells was checked with type-specific antibodies in flow cytometry analysis (see column 12, lines 50-64, in particular). Antibodies specific for CD3, CD4 and CD8 were used to detect and characterize cells, which were obtained from the $CD34^+$ population (see column 12, lines 49-67), which reads on a plurality of cells selected to render the unit suitable for therapy (claim 16).

If $CD34^+$ cells are separated from the original blood sample, than many or a plurality of cell types have been removed from the unit. Therefore, Johnson et al teach a cytotherapeutic unit comprising cells from a mixture of cord blood or postpartum placenta wherein a plurality of cells have been removed from the unit (claims 31-32). The expanded and differentiated cell population containing $CD34^+$ cells obtained from both cord blood and placental blood (i.e. two sources) taught by Johnson et al anticipates the claimed cytotherapeutic unit comprising a mixture of cells obtained from cord blood and placenta, said cells comprising a plurality of different cell types (i.e. CD3, CD4, CD8 and CD34, at least one cell obtained from a source that differs from a source of another type (claim 34).

As discussed above, limitations in claims 20-23 and 50 are drawn to knowledge concerning the cytotherapeutic unit, such as the identity and numbers of the cells in the unit, assurance that the assays are accurate. The identities and numbers of at least some of the cells in the cytotherapeutic unit is an inherent property of the unit. Whether

the assay to determine the identities and numbers of the cells is accurate or not is an inherent property of the assay. Absence of particular cell types from a cytotherapeutic unit is an inherent property of the cytotherapeutic unit. In other words, certain cell types are present in the unit or they are not. Either the particular cytotherapeutic unit for an indicated disease state or condition is suitable based on the cell content or it is not suitable. Knowledge of the cells does not alter the properties of the claimed cytotherapeutic unit. See MPEP 2112. Therefore, the hematopoietic cells in the preparations taught by Johnson et al would have numbers and identities, and the assays performed by Johnson et al to determine numbers and viability would or would not be accurate. In order for the hematopoietic cell preparations taught by Johnson et al to anticipate the claimed cytotherapeutic unit, it is not necessary for the Johnson et al to have known the identities and numbers of at least some of the plurality of cells or to know or certify the accuracy of the assay.

Johnson et al do not teach a library of cytotherapeutic units. Johnson et al do not teach use of a post partum placenta perfusate. The teaching of Fasouliotis et al has been discussed in the above rejection.

It would have been obvious to the skilled artisan at the time the invention was made to produce a library or bank of the donor samples such as produced by Johnson et al because Fasouliotis et al teach that many blood samples can be collected from cord blood and a saline flush of postpartum placenta enriched for CD34+ cells and stored in a bank so that they will be available for a patient in need of hematopoietic cells. The motivation to make a library or bank of the donor samples as taught by

Fasouliotis et al is the expected benefit of having easy access to blood samples, increased speed of donor search, viral safety and having a source of stem cells for expansion and gene therapy. A further benefit would be the ability to expand available donor pools in currently under-represented ethnic and racial minorities (see page 14, left column, 3rd paragraph, for example). There is a reasonable expectation of success in making a library or bank of the cytotherapeutic units taught by Johnson et al since it has worked previously as described by Fasouliotis et al.

It would have been obvious to the skilled artisan at the time the invention was made to perfuse the postpartum placenta as taught by Fasouliotis et al to collect cells for a therapeutic cell composition such as produced by Johnson et al because Fasouliotis et al teach that there is a relatively small number of cells in a sample of umbilical cord blood. The motivation to use postpartum placenta perfusate is the expected benefit of being able to collect additional blood as disclosed by Fasouliotis et al (see Table 2, page 15, in particular). There is a reasonable expectation of success in using postpartum placenta perfusate to increase cell number in cytotherapeutic units since it has worked previously as described by Fasouliotis et al. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fasouliotis et al (Eur. J. Obstet. Gynecol. Reprod Biol., 2000, Vol. 90, pages 13-

25) as applied to claim 1 herein above in view of Ende et al (Life Sciences 2001, of record).

Applicant claims a cytotherapeutic unit, wherein the potent cells are obtained from at least two individuals or at least five individuals.

The teachings of Fasouliotis et al are described in the above rejections. Fasouliotis et al do not teach a cytotherapeutic unit wherein the potent cells are obtained from at least two individuals or at least five individuals.

Ende et al teach a method of pooling umbilical cord samples before administration to reconstitute bone marrow after exposure to radiation. Ende et al discloses that a barrier to use of umbilical cord blood is that it is difficult to obtain enough stem cells for effective grafting especially since adults require many more stem cells. Ende et al also discloses an additional difficulty related to variability in the volume and quantity of cord blood samples (see page 1532, 1st paragraph, for example). Ende et al teach that fifteen human umbilical cord blood samples were obtained from full term neonates and that five milliliters of each were mixed in combination with two or three different other specimens (see page 1533, 2nd paragraph, for example). Ende et al teach that combined cord blood samples had an increase in percentage of colony forming units and a significant increase in the number of primitive colonies and CD34+ cells when compared to individual samples stored in the same manner (see page 1534, 3rd paragraph and Table 2, for example).

It would have been obvious to combine the teaching of Ende et al to use samples of cord blood from two or more individuals with the hematopoietic cell composition of

Fasouliotis et al to make a cytotherapeutic unit wherein cells are obtained from at least two individuals or at least five individuals because Ende et al discloses that more cells can be obtained from multiple samples to provide adequate number of stem cells for therapy. The motivation to do so is the expected benefit of as suggested by Ende et al and Fasouliotis et al being able to use cells from at least two individuals or at least five individuals to provide sufficient cells in therapeutic hematopoietic products for all patients, including adults or children of different ethnic origins. There is a reasonable expectation of success in using cells obtained from at least two individuals or at least five individuals because Ende et al teach that there is an increase in cell number after combination of samples and therapeutic hematopoietic products have worked previously as taught by Fasouliotis et al. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 1, 3, 5-6, 8, 12, 15-18, 20-23, 31-32, 34- 37 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al (U.S Patent No. 5,677,139, of record) in view of Wang et al (Blood, 2001 Vol. 98 (No. 11 Part 1) page 193 (abstract only)).

The teachings of Johnson et al are described in the above rejection. Johnson et al do not teach a cytotherapeutic unit comprising cell from postpartum perfusate.

Wang et al teach a method to recover mononucleated cells and hematopoietic progenitor and stem cells (HPSC) from postpartum human placenta by perfusing the placenta to remove residual blood, and then continuously perfusing at a controlled rate until 200 to 250 ml of postpartum placenta perfusate was collected. Wang et al teach that populations of HPSC that were characterized as $CD34^+$ $CD38^+$ cells were recovered in numbers comparable to the number of cells recovered from a typical unit of umbilical cord blood, but with a significantly higher proportion of $CD34^+CD38^-$ cells. Wang et al conclude that HPSC from postpartum placenta may be used to supplement umbilical cord blood to yield sufficient graft material for transplantation into adults (see full abstract, in particular).

It would have been obvious to the skilled artisan at the time the invention was made to collect hematopoietic cells from a postpartum placenta perfusate as taught by Wang et al to add to a cell sample for therapeutic use as taught by Johnson et al because Wang et al teaches that postpartum placenta perfusate yields a useful quantity of $CD34^+CD38^-$ cells, which is a cell subpopulation believed to contain long term repopulating activity. The motivation to use postpartum placenta perfusate as an additional source of $CD34^+$ hematopoietic cells for a therapeutic transplant sample is the expected benefit of being able to have a sufficient volume of therapeutic cells to meet the cell dose requirements of adult hematopoietic cell transplant recipients as suggest by Wang et al. There is a reasonable expectation of success to collect and use cells from a postpartum placenta perfusate for a cytotherapeutic unit since it has worked previously in the cited reference. Given the teachings of the prior art and the level of

skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Laura McGillem, PhD
12/20/2006

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